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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,829	02/25/2000	David S. Garvey		6724

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EDWARD D GRIEFF
HALE & DORR LLP
1455 PENNSYLVANIA AVE, NW
WASHINGTON, DC 20004

EXAMINER

RAO, DEEPAK R

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 07/02/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/512,829

Applicant(s)
Garvey et al.

Examiner
Deepak Rao

Art Unit
1624



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Apr 10, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 36-45, 50, 51, 59, 60, 64, 66, 68, and 79-118 is/are pending in the application.
- 4a) Of the above, claim(s) 42-45, 112, and 116 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-41, 50, 51, 59, 60, 64, 66, 68, 79-111, 113-115, 117, and 118 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 22 6) ☐ Other:

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DETAILED ACTION

This office action is in response to the amendment filed on April 10, 2003.

Claims 36-45, 50, 51, 59, 60, 64, 66, 68 and 79-118 are pending in this application.

Election/Restriction

Applicant is reminded that the prosecution of the instant application is based on the election of the species of **lansoprazole** as the proton pump inhibitor and **S-nitrosogluthathione** as the compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium derived relaxing factor, or a substrate of nitric oxide synthase. As the respective species were found in the prior art, the examination was limited to the elected species. MPEP § 803.02.

Claims 42-45, 112 and 116 drawn to other compounds that donate, transfer, or release nitric oxide, etc., and the remaining proton pump inhibitor compounds and NO donating compounds from the claims under consideration (i.e., claims 50-51, 59-60, 64, 66, 68, 36-41, 79-111, 113-115 and 117-118) are additionally withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species.

Inventorship

In view of the papers filed July 16, 2001, the inventorship of this nonprovisional application has been changed by the deletion of Tiansheng Wang and Stewart K. Richardson.

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The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and USPTO PALM data to reflect the inventorship as corrected.

The following rejections are maintained:

Claims 50-51, 59-60, 64, 66, 68, 36-41 and 79-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Nohara et al., U.S. Patent No. 4,628,098 or Depui et al., WO 97/25064 or WO 96/24375] and Stamler et al., U.S. Patent No. 5,380,758; for the reasons provided in the previous office action which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant first argues that independent claims 50 and 64 specifically refer to 'improving the gastroprotective properties', etc. of the proton pump inhibitor and the references do not disclose or suggest such methods. However, the references clearly teach therapeutic administration of lansoprazole in a method to achieve the benefit of treating gastrointestinal diseases, which is the same therapeutic benefit achieved in the instant claims. The preamble language is not given any patentable weight.

Next, applicant argues that Stamler reference teaches the use of S-nitrosothiols for relaxing gastrointestinal smooth muscle and applicant's presently claimed methods are unrelated to such activity. However, Stamler clearly teaches the use of S-nitrosothiols in treating gastrointestinal diseases, see col. 9, lines 34+. Stamler teaches the therapeutic administration of

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S-nitrosothiol compounds in a method to achieve the benefit of treating gastrointestinal diseases, which is the same benefit sought in the instant claims. The specific recitation of improving various properties of the proton pump inhibitor is not given any patentable weight. The references individually teach administration of the compounds to achieve the same therapeutic benefit and therefore, there is sufficient motivation to one of ordinary skill in the art to combine the same.

Applicant submits that Depui reference teaches proton pump inhibitors in combination with NSAID compounds or an antacid formulation and their methods of use for treating gastrointestinal disorders, but argues that the reference does not teach or suggest the use of compounds of the instant claims that donate, transfer or release nitric oxide. However, Stamler in analogous art teaches the use of such compounds in the treatment of gastrointestinal disorders and thus, the motivation to combine the references flows logically from their having been individually taught in the prior art.

Applicant lists the various diseases specifically recited in claim 59 and argues that 'there is no evidence of record of any relationship between Stamler's disclosed method and the claimed methods'. This is not found to be persuasive because Stamler clearly teaches the use of the compounds in treating gastrointestinal disorders which include those of the esophagus, duodenum, sigmoid colon, etc. (see col. 9, lines 34-47). The instant claims also recite **gastroesophageal** reflux disease, colitis (i.e., inflammation of the mucous membrane of the

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colon), duodenal ulcer, etc. which involve the specific target areas discussed in Stamler and applicant has not provided any evidence to the contrary.

Applicant argues that the references Nohara and WO 96/24375 do not disclose or suggest a method for 'decreasing or reversing gastrointestinal toxicity' etc. However, the references clearly teach therapeutic administration of lansoprazole in a method to achieve the benefit of treating gastrointestinal diseases, which is the same therapeutic benefit achieved in the instant claims. The preamble language is not given any patentable weight. Further, applicant submitted in the response of paper no. 16 (filed March 25, 2002) that 'each of the specific methods of the independent claims are all related as they are directed to methods for the treatment and/or prevention of a gastrointestinal disorder'.

Next, applicant argues that Nohara and WO 97/25064 are unrelated to methods of treating infections by *H. pylori*. However, WO 96/24375 teaches the use of proton pump inhibitors in a method of treating *Helicobacter* infections using and further, the reference discloses that 'the relationship between gastrointestinal disorders and infections with *Helicobacter pylori* is well established'. Therefore, there is sufficient motivation to the skilled artisan to combine these teachings with Stamler as the references individually teach the use of the respective compounds for the treatment of gastrointestinal disorders. Applicant has not provided any evidence to show unexpected synergistic effect for the combination.

Accordingly, the rejection of the previous office action is maintained.

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The following rejections are necessitated by the amendment:

Claim Rejections - 35 U.S.C. § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 85-100 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Nohara et al., U.S. Patent No. 4,628,098 or Depui et al., WO 97/25064 or WO 96/24375] and Stamler et al., U.S. Patent No. 5,380,758.

Nohara et al. (US'098), teaches benzimidazole compounds including lansoprazole that are useful in treating gastrointestinal disorders and digestive ulcers, see formula (I) in the reference and the specific compound in claim 10.

Depui et al. (WO'064) teaches proton pump inhibitors that are useful in the treatment of gastrointestinal disorders and exemplifies lansoprazole (see page 10, second compound). WO'064 teaches the combination of the proton pump inhibitor with a NSAID, which NSAID's include selective COX-2 inhibitors and NO releasing NSAID's (see page 13, lines 1-2) and antacid formulations (see page 17, lines 7+), however, the reference does not exemplify a S-nitrosothiol.

Also, see WO'375 which discloses lansoprazole (page 8, third compound) and teaches the use of the proton pump inhibitor compounds in treatment of disorders associated with *Helicobacter pylori*. Further, WO'375 teaches that combination therapy of these diseases with bismuth compounds, see page 1, second paragraph.

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Stamler et al., US'758 in the analogous art teaches S-nitrosothiols including S-nitrosoglutathione (see col. 10, line 36) that have gastrointestinal therapeutic activity (see col. 9, lines 34-47). Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of the above references because he would have had the reasonable expectation that the composition comprising the individual compounds of the references would have the same therapeutic activity as taught for each of the compounds. [T]he idea of combining the references flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

With respect to the specific remarks regarding the independent claims 85, 87, 89 and 94, applicant's attention is directed to the reasons provided above.

2. Claims 101-111, 113-115 and 117-118 are rejected under 35 U.S.C. 103(a) as being unpatentable over [Nohara et al., U.S. Patent No. 4,628,098 or Depui et al., WO 97/25064] in combination with Stamler et al., U.S. Patent No. 5,380,758.

Nohara et al. (US'098), teaches benzimidazole compounds including lansoprazole that are useful in treating gastrointestinal disorders, see formula (I) in the reference and the specific compound in claim 10. Also, Depui et al. (WO'064), teaches proton pump inhibitors useful in the treatment of gastrointestinal disorders and exemplifies lansoprazole (see page 10, second compound). WO'064 teaches the combination of the proton pump inhibitor with a NSAID, which NSAID's include selective COX-2 inhibitors and NO releasing NSAID's (see page 13,

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lines 1-2) and antacid formulations (see page 17, lines 7+), however, the reference does not exemplify a S-nitrosothiol. Stamler et al., US'758 in the analogous art teaches S-nitrosothiols including S-nitrosoglutathione (see col. 10, line 36) that have gastrointestinal therapeutic activity (see col. 9, lines 34-47). Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of the above references because he would have had the reasonable expectation that the composition comprising the individual compounds of the references would have the same therapeutic activity as taught for each of the compounds. [T]he idea of combining the references flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Receipt is acknowledged of the Information Disclosure Statements filed on April 10, 2003 and copy is enclosed herewith.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after


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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


Deepak Rao
Primary Examiner
Art Unit 1624

June 30, 2003